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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,072	07/02/2001	William M. Canfield	210119US0CONT	3250

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EXAMINER

PATTERSON, CHARLES L JR

ART UNIT PAPER NUMBER

1652

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/895,072

Applicant(s)

CANFIELD, WILLIAM M.

Examiner

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-42 and 45-72 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-32, 35-42, 45-58 and 63-72 is/are rejected.
- 7) ☒ Claim(s) 33, 34 and 59-62 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Claims 39, 42, 45, 46 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is indefinite in the recitation of "said modified lysosomal hydrolases" on lines 5-6, which lacks antecedent basis. The claim is also incorrect in the recitation of "hydrolases" on line 6, which should be "hydrolase". Applicant did not address this rejection in the instant amendment.

Claims 42, 45 and 46 are confusing and apparently incorrect in the recitation of " α -N-Acetylglucosaminidase", which apparently should be " α -N-Acetylglucosaminidase". Applicants corrected this in some claims but did not correct it in these claims.

Claim 50 is incorrect in the recitation of "hydrolases" on line 9, which should be "hydrolase". This rejection is not addressed in the instant amendment.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The previous 103(a) rejection over Kornfeld, et al. (BW) is hereby dropped. The examiner apparently confused the enzyme whose purification was taught in that reference.

Claims 25-32, 35-38, 50-58 and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Kornfeld (AY-2 or AZ-2) or Cuzzo

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(AX-2) in view of Bao, et al. (U). The primary references teach that lysosomal enzymes must be phosphorylated by mannose 6-phosphate in order to be recognized by the receptors in the lysosomal membrane and thus be transported inside. They further teach that two enzymes are involved, first N-acetylglucosamine-1-phosphotransferase and then N-acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase. Bao, et al. teach a method of purifying the N-acetylglucosamine-1-phosphotransferase to 1,900,000 units/ml, which is defined in column 1 of page 31438 as being 1,900,000 pmol/h/mg, by the use of a monoclonal antibody. It would have been obvious to one of ordinary skill in the art to phosphorylate lysosomal hydrolases using these two enzymes, absent unexpected results. The other requirements of the instant claims would have been obvious, absent convincing proof to the contrary. The motivation would have been to study the uptake of the enzyme into the lysosome and/or the effect of lysosomal diseases.

The examiner, in trying to consolidate the 1449's from 09/865,552 and this application, cited the wrong Bao, et al. reference in the previous rejection and for that reason this action is made non-final. As with Kornfeld, et al. (BW), applicants argue that "on page 31438, bottom of col. 2, the protocol used to identify the one antibody from a pool of millions of possible hybridoma cell lines required numerous steps and screenings [and] [i]t is unlikely that one could successfully reproduce the protocol and, in fact, obtain the same antibody needed to purify the enzyme to such a high purity and specific activity". The "required numerous steps and screenings" needed are taught by the instant published reference. It is maintained that the N-acetylglucosamine-1-phosphotransferase could have been purified to the claimed purity using this reference, absent very convincing proof to the contrary. This should probably be in a 132 declaration by someone other than the inventor

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who has tried the method taught by Bao, et al. (U) and has been unable to obtain the antibody and purify the enzyme. The reference is deemed to teach one of ordinary skill in the art to do the purification within the bounds of routine experimentation, which for an antibody and enzyme purification might entail considerable experimentation, but with the guidance provided by the reference.

Claims 39-42 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kornfeld, et al. (BW). Kornfeld, et al. teach that lysosomal enzymes must be phosphorylated by mannose 6-phosphate in order to be recognized by the receptors in the lysosomal membrane and thus be transported inside. They further teach that two enzymes are involved, first N-acetylglucosamine-1-phosphotransferase and then N-acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase and they teach the purification of N-Acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase to a purity of 498,500 units/mg (see Table III, page 23207). It would have been obvious to one of ordinary skill in the art to phosphorylate lysosomal hydrolases using these two enzymes, absent unexpected results. The other requirements of the instant claims would have been obvious, absent convincing proof to the contrary. The motivation would have been to study the uptake of the enzyme into the lysosome and/or the effect of lysosomal diseases. Applicants arguments concerning the rejection over this reference were directed to different claims and they further argue that "on page 23205, bottom of col. 2, the protocol used to identify the one antibody from a pool of millions of possible hybridoma cell lines required numerous steps and screenings [and] [i]t is unlikely that one could successfully reproduce the protocol and, in fact, obtain the same antibody needed to purify the enzyme to such a high purity and

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specific activity". To start with, apparently applicants intended to refer to the bottom of page 23204, not 23205. Secondly, the "required numerous steps and screenings" needed are taught by the instant published reference. It is maintained that the N-Acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase could have been purified to the claimed purity using this reference, absent very convincing proof to the contrary. This should probably be in a 132 declaration by someone other than the inventor who has tried the method taught by Kornfeld, et al. (BW) and has been unable to obtain the antibody and purify the enzyme. The reference is deemed to teach one of ordinary skill in the art to do the purification within the bounds of routine experimentation, which for an antibody and enzyme purification might entail considerable experimentation, but with the guidance provided by the reference.

Claims 69-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kornfeld, et al. (BW) in view of Bao, et al. (U). As noted previously, Kornfeld, et al. teach that lysosomal enzymes must be phosphorylated by mannose 6-phosphate in order to be recognized by the receptors in the lysosomal membrane and thus be transported inside. They further teach that two enzymes are involved, first N-acetylglucosamine-1-phosphotransferase and then N-acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase and they teach the purification of N-Acetylglucosamine-1-phosphodiester α -N-acetylglucosaminidase to a purity of 498,500 units/mg (see Table III, page 23207). Bao, et al. teach a method of purifying the N-acetylglucosamine-1-phosphotransferase to 1,900,000 units/ml, which is defined in column 1 of page 31438 as being 1,900,000 pmol/h/mg, by the use of a monoclonal antibody. It would have been obvious to one of ordinary skill in the art to phosphorylate lysosomal hydrolases using these two enzymes, absent unexpected results. The other require-

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ments of the instant claims would have been obvious, absent convincing proof to the contrary. The motivation would have been to study the uptake of the enzyme into the lysosome and/or the effect of lysosomal diseases.


The arguments concerning this rejection are discussed in the two previous rejections and incorporated here. The only difference in these claims and the two previous sets of claims is that they require both enzymes to be purified and not just one.

Claims 33, 34, and 59-62 are objected to as being dependent upon a rejected base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
May 28, 2003